REMARKS

Claims 1-2, 22, 25, and 31-32 are presently pending. New claims 33-39 are supported by the specification and do not contain new matter.[1]

I. 35 U.S.C. §112, First Paragraph, Enablement Rejections

Reconsideration is requested of the rejection of claims 1, 2, 22, 25, and 31-32 under 35 U.S.C. 112, first paragraph. The Office has asserted that these claims are not sufficiently enabled by the specification.

Claim 1 is directed toward a method to treat a herpetoviridae infection in a subject by administering to the subject a sulfur-containing compound. The sulfur-containing compound, as recited in claim 1, inhibits **both** a (H^+/K^+) ATPase and a herpetoviridae protease.

The standard for enablement is whether one of ordinary skill in the art could make or use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation.[2] In this case, the specification coupled with information generally known in the art, fully enables a person of ordinary skill to identify and prepare sulfur-containing compounds that inhibit both a (H^+/K^+) ATPase and a herpetoviridae protease for use in the method of claim 1 **without undue experimentation**. The specification details numerous embodiments of sulfur-containing compounds that may be employed in the method of claim 1. According to the specification, the sulfur-containing compound may be a compound having any of the following general formulas I[3], II[4], or III[5]:

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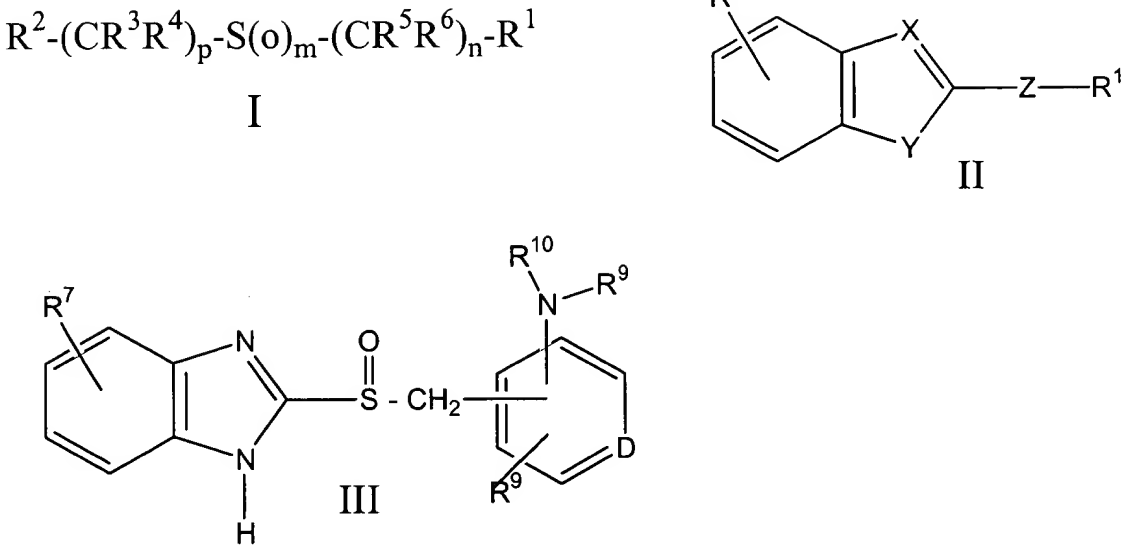
[1]Support for benzimidazoles, as detailed in Paper 10 at page 3, can be found on pages 71-128 of the specification.

[2]U.S. v. Teletronics, Inc., 8 USPQ2d 1217 (Fed. Cir. 1988).

[3]Compounds having formula I are detailed on pages 6-24 of the specification.

[4]Compounds having formula II are detailed on pages 24-39 of the specification.

[5]Compounds having formula II are detailed on pages 39-45 of the specification.



The specification also details well over 300 examples of specific compounds having formula I, II or III.[6] In addition, the specification discloses five general reaction schemes that may be utilized to prepare compounds having formula I, II, or III[7] along with over 100 examples of compounds that were made following the steps of one of the five general schemes. Moreover, the specification discloses biological data showing the ability of tested compounds to inhibit **both** a (H$^+$/K$^+$) ATPase and a herpetoviridae protease[8] as well as detailed assays that fully enable a skilled artisan to determine the ability of any particular compound to inhibit **both** a (H$^+$/K$^+$) ATPase and a herpetoviridae protease[9]. In view of this disclosure, selecting an appropriate sulfur-containing

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[6]See pages 11-24 of the specification.

[7]General reaction schemes one through five are disclosed on pages 56-64 of the specification. Examples of specific compounds prepared by one of these reaction schemes are disclosed on pages 71-129 of the specification.

[8]Assays evaluating the ability of compounds to inhibit a (H$^+$/K$^+$) ATPase are disclosed on pages 111-137 of the specification. Assays evaluating the ability of compounds to inhibit a protease are detailed on pages 137-144 of the specification.

[9]Assays evaluating the ability of compounds to inhibit a (H$^+$/K$^+$) ATPase are disclosed on pages 111-137 of the specification. Assays evaluating the ability of compounds to inhibit a protease are detailed on pages 137-144 of the specification.

compound was clearly described in a manner so as to enable a skilled artisan to make and use the method of claim 1 without undue experimentation.

According to the Office, however, claim 1 is not enabled because an undue amount of experimentation would be required to determine whether a particular sulfur-containing compound could be used for treating a herpetoviridae infection in light of the existence of "millions of sulfur containing compounds...which may or may not treat herpetoviridae infection." [10] In arriving at this conclusion, the Office relied on In re Wands.[11] In the Wands case, the claim at issue required using an antibody "wherein said antibody is a monoclonal high affinity IgM antibody having a binding affinity constant for said HBsAg determinants of at least 10^9M^{-1}."[12] The Federal Circuit discussed several of the relevant factors, and concluded that "undue experimentation would not be required to practice the invention."[13] Contrary to the Office's assertion, however, Wands supports the conclusion that claim 1 is sufficiently enabled. Each of the factors considered by the Federal Circuit in the Wands case is discussed below.[14]

With regard to the factor of "the amount of direction provided by the inventor," the Federal Circuit concluded that Wands provided "significant guidance and direction on how to practice the invention and present[ed] working examples." The Wands patent (4,879,219) is 18 columns long, including two columns of claims. Applicants' present specification is 144 pages long prior to the claims, including 88 pages (56-144) devoted to synthesis, working examples, and screening. The present specification provides five general schemes for the preparation of sulfur-containing compounds having formulas I, II or III generally, as well as for the preparation of particular classes of compounds within the scope of each formula, in addition to intermediates useful in their preparation and the specification discloses over 100 examples illustrating the preparation of particular species within the scope of formula I, II or III. One skilled in the art, equipped with the detailed disclosure of the instant specification, and familiar

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[10]See Paper 10 at page 2.

[11]In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

[12]*Id.*, at 8 USPQ2d p. 1402.

[13]*Id.*, at 8 USPQ2d p. 1406.

[14]The factors include: nature of the invention, breath of the claims, guidance in the specification, working examples, state of the art, predictability of the art, the quantity of experimentation necessary.

with basic synthetic organic chemistry, could readily adapt the synthetic schemes and examples described in the specification to prepare, select and test compounds within the scope of claim 1. Such adaptation is clearly within the abilities of one skilled in the art, and while some experimentation may be needed, such experimentation could be routinely performed by the skilled artisan, i.e., the adaptation could be accomplished without undue experimentation.

With regard to "the level of skill," the Federal Circuit stated "There was a high level of skill in the art at the time when the application was filed."[15] In the present situation, the level of skill of pharmaceutical chemists in the field of chemical synthesis is similarly high.

With regard to "the nature of the invention," the Federal Circuit in Wands stated that

> the nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody.

Similarly in the present case, the nature of the invention requires reasonable screening, and pharmaceutical chemists in the field of chemical synthesis are prepared to screen sulfur-containing compounds falling within the claim scope .

With regard to "working examples," Wands conducted just ten fusion experiments to produce hybridomas having the required binding affinity[16], and carried out the entire synthesis and screening procedure just three times.[17] The present specification provides 111 detailed working examples of syntheses and tested 57 compounds for their ability to inhibit a (H^+/K^+) ATPase[18] and 17 compounds for their ability to inhibit a herpetoviridae protease[19] . This cannot fairly be deemed to favor a finding of non-enablement.

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[15]In re Wands, 8 USPQ2d 1406.

[16]*Id.*, at 8 USPQ2d 1405.

[17]*Id.*, at 8 USPQ2d 1407.

[18]See Table 1 at pages 134-136 of the specification.

[19]See Table 2 at page 142 of the specification.

With regard to "state of the art," the state of the art is especially well developed in the fields of chemical synthesis and screening for pharmaceutical activity.

With regard to the "breadth of the claims," the Federal Circuit noted that of 143 candidate antibodies produced by Wands, his testing of just nine and proving the required activity of just four, not even considering countless others which Wands did not make, was sufficient to support claims of the following breadth: "wherein said antibody is a monoclonal high affinity IgM antibody having a binding affinity constant for said HBsAg determinants of at least 10^9M^{-1}."[20] This breadth, deemed acceptable, is much broader than a claim limited to those antibodies that Wands either produced or tested. Against this background, the breadth of claim 1 is reasonable in light of the 144 pages of explanatory specification including 88 pages devoted to synthesis, working examples, detailed biological screening of synthesized compounds, and detailed assays that fully enable a skilled artisan to screen putative sulfur containing compounds for their ability to inhibit both a (H^+/K^+) ATPase and a herpetoviridae protease .

With regard to the "level of predictability," the Federal Circuit in Wands noted that viewing the data as proposed by the Board, only four of 143 of Wands' hybridomas, or 2.8% of those produced (not even considering those not produced), were proven to have the activity required by the claims.[21] In the present specification many more candidates than four were tested (i.e., 57), and screening according to the procedures in the specification is well within the ordinary skill in the art.

With regard to the "quantity of experimentation," in Wands nine of 143 hybridomas were tested, and four were determined to have the required activity. This left 130+ hybridomas produced untested, as well as countless others not even produced. The present applicants should similarly not be precluded from patent protection on the basis they have left a considerable quantity of compounds untested, because, as stated by the Board:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.[22]

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[20] In re Wands, at 8 USPQ2d 1405.

[21] *Id.*, at 8 USPQ2d 1405.

[22] Ex parte Forman, 230 U.S.P.Q. 546, 547 (BPAI 1986); see also MPEP 2164.06.

Patent applicants are not required to show a specific example for every possible embodiment of the claimed invention, so long as the specification and the general knowledge of the art would enable one of ordinary skill in the art to make and use the invention.[23]

For the foregoing reasons, the Office has failed to establish that claim 1 is not sufficiently enabled. Moreover, claims 2, 22, 25, 31, 32, and new claim 33, which depend from claim 1, are likewise enabled for all of the reasons detailed regarding claim 1.

II. 35 U.S.C. §102 (b) Rejection

Reconsideration is requested of the rejection of claims 1, 2, 22, 25, 31, and 32 under 35 U.S.C. §102(b) as anticipated by EP 0 407 217 (EP '217).

Claim 1 is directed toward a method to treat a herpetoviridae infection in a subject by administering to the subject a sulfur-containing compound. The sulfur-containing compound, as recited in claim 1, inhibits **both** a (H^+/K^+) ATPase and a herpetoviridae protease.

EP '217 generally discloses a class of compounds that are said to have antiviral activity, antiinflammatory activity, and that are platelet activating factor inhibitors.

Nowhere does EP '217 disclose or suggest sulfur-containing compounds that are dual inhibitors of **a (H^+/K^+) ATPase** and **a herpetoviridae protease**, as required by claim 1. A claim is anticipated only if each and every element as set forth in the claim is described in a single prior art reference.[24] Because EP '217 does not disclose every element of claim 1, the reference does not anticipate claim 1.

The Office, however, asserts that EP '217 discloses "treatment of herpetoviridae infection using sulfur containing compounds" and that inhibition of a (H^+/K^+) ATPase and a herpetoviridae protease by the compounds disclosed in EP '217, and in particular example 30, "is inherent."[25]

To properly support a determination of inherency, as a matter of Patent Office practice, it is incumbent on the Office to first provide rationale or evidence tending to show inherency.[26] In establishing this rationale or evidence, the Examiner must provide a basis in fact and/or technical reasoning to support the determination that the

[23] In re Borkowski, 164 U.S.P.Q. 642, 645 (CCPA 1970).

[24] Verdegaal Bros. v. Union Oil Co. of Calif., 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987). See MPEP §2131.

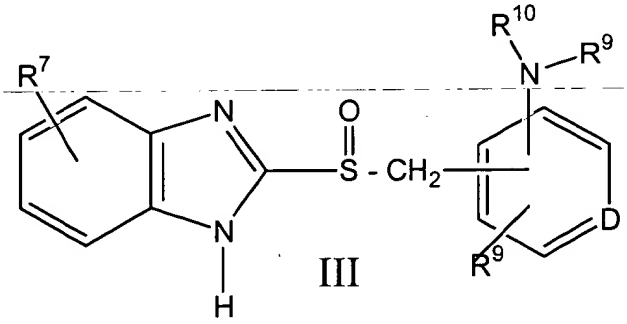
[25] Paper 10 at page 4.

[26] See MPEP § 2112.

allegedly inherent characteristic necessarily flows from the teaching of the cited art.[27] Furthermore, the mere fact that a certain characteristic may be present in the prior art is not sufficient to establish the inherency of that characteristic. Only after this initial burden of proof has been met by the Office, does the burden shift to the Applicant.

Against the backdrop of this legal standard, the Office has not properly supported its determination of inherency. The Office has merely stated "inasmuch as the structure of the compounds are similar [i.e., the compounds disclosed in the present invention and Example 30 of EP '217], the disease is the same, it will be expected that the compounds will have the same mechanism, i.e., inhibition of herpetoviridae protease."[28] No rationale or evidence has been provided by the Office to support this conclusion.

The cited art of record, in fact, casts doubt upon the conclusions relied upon by the Office in arriving at its inherency rejection in view of the known structure and function of several disclosed prior art compounds. One sulfur containing compound detailed in the present specification as suitable for use in the method of claim 1 and cited by the Office, is a benzimidazole compound having the following general formula III:



III

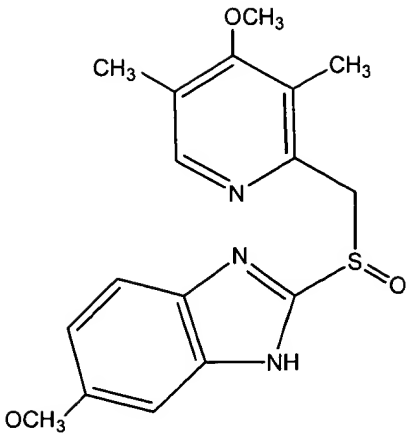
Compounds having formula III are disclosed in the present specification as inhibitors of **both** a (H^+/K^+) ATPase and a herpetoviridae protease.

Lindberg et al.,[29] a reference cited by the Office in its obviousness rejection, disclose a gastric acid secretion inhibitor, omeprazole, having the formula:

[27]Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

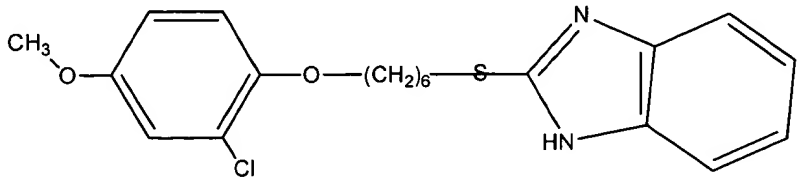
[28]Paper 10 at page 5.

[29]Lindberg et al., (1987) TIPS 8:399-402.



Lindberg et al. disclose that omeprazole is a (H^+/K^+) ATPase inhibitor. But nowhere does Lindberg et al. disclose that omeprazole is an inhibitor of a herpetoviridae protease. To the contrary, Table 2 in the present specification details results comparing the ability of a number compounds that are (H^+/K^+) ATPase inhibitors to inhibit assemblin (i.e., a serine viral protease). One of the compounds tested was omeprazole and it was found to have 0% assemblin inhibition activity.[30] Despite being structurally similar to benzimidazole compounds of the current invention having formula III, omeprazole does not have the same function.

The compound disclosed by EP '217 in Example 30 (i.e., the compound referenced by the Office in its inherency rejection) has the following structure:



The compounds disclosed in EP '217 are said to have antiviral activity, antiinflammatory activity, and are said to be platelet activating factor inhibitors. Nowhere, does EP '217 disclose or suggest that any disclosed compound (including Example 30) has the ability to inhibit both a (H^+/K^+) ATPase and a herpetoviridae protease. The Office, as detailed above, has stated that because Example 30 is structurally similar to benzimidazole compounds having formula III "it will be expected that the compounds will have the

[30]See page 142 of the specification.

same mechanism, i.e., inhibition of herpetoviridae protease."[31] In light of the fact that omeprazole is structurally more similar to benzimidazole compounds having formula III than is the compound of Example 30, and yet does not inhibit assemblin (i.e., a serine viral protease), serious doubt is cast upon the Office's conclusion that the compound of Example 30 inherently has the same function as benzimidazole compounds having formula III.

For the foregoing reasons, the Office has failed to establish that claim 1 is anticipated by the disclosure of EP '217. Moreover, claims 2, 22, 25, 31, 32, and new claim 33, which depend from claim 1, are patentable over the cited art for all of the reasons identified for claim 1 and by reason of the additional requirements that they introduce.

III. 35 U.S.C. 103(a) Rejection

Reconsideration is requested of the rejection of claims 1-2, 22, and 25 under 35 U.S.C. §103(a) in view of EP 0 407 217 ('217) and Lindberg et al.[32]

Lindberg et al. disclose a class of gastric acid secretion inhibitors, omeprazole, which prevent gastric acid secretion by inhibiting the gastric H^+/K^+ ATPase.[33] According to Lindberg et al., the primary use of the compounds is for the treatment of **gastric ulcers**.[34] Lindberg et al. do not disclose or suggest a method to treat **herpetoviridae infection**. Lindberg et al. also do not disclose or suggest sulfur-containing compounds that are dual inhibitors of **a (H^+/K^+) ATPase** and **a herpetoviridae protease**, as required by claim 1.

EP '217 generally discloses a class of compounds that are said to have antiviral activity, antiinflammatory activity, and that are platelet activating factor inhibitors. Nowhere does EP '217 disclose or suggest sulfur-containing compounds that are dual inhibitors of **a (H^+/K^+) ATPase** and **a herpetoviridae protease**, as required by claim 1.

In the absence of any disclosure of these elements of the method defined in claim 1, a *prima facie* case for obviousness is lacking.

According to the Office, it would have been *prima facie* obvious "to use the Lindberg et al. compounds for treating herpes infection, as taught by EP '217, because the latter reference expressly teach that the benzimidazole class of compounds

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[31]Paper 10 at page 5.

[32]Lindberg et al., (1987) TIPS 8:399-402.

[33]Lindberg et al. see abstract.

[34]*Id.*

containing sulfur are known to treat herpes."[35] There is no motivation, either express or implied in the references themselves or offered by the Office as to why a skilled artisan would make the Office's proposed substitution. Accordingly, a skilled artisan empowered with the cited art cannot fairly be deemed to be motivated to substitute the anti secretory, sulfur-containing compounds disclosed by Lindberg et al. for the antiviral, sulfur-containing compounds disclosed in EP '217 to treat a herpetoviridae infection. As stated in MPEP 2143, where there is no motivation to modify a reference as proposed, the proposed modification is not obvious.

Moreover, as set-forth in II. above, Table 2 in the present specification details results comparing the ability of a number compounds that are (H^+/K^+) ATPase inhibitors to inhibit assemblin (i.e., a serine viral protease). One of the compounds tested was omeprazole (i.e., the compound disclosed by Lindberg et al.) and it was found to have 0% assemblin inhibition activity.[36] If a skilled artisan had made the Office's proposed substitution, accordingly, they would not have arrived at the method of claim 1.

The Office, however, asserts that it is not relevant that the cited art make no mention of treatment of infection caused by herpetoviridae virus infection because "discovery of a new benefit for an old process does not render the old process patentable" based upon the theory of inherency.[37] For all of the reasons detailed in II. above, the Office has not sufficiently supported a determination of inherency. Additionally, Applicant's have not simply discovered a new property inherent to a process disclosed in the cited art. Claim 1 is directed toward a method to treat **herpetoviridae infection** by administering a compound that is a dual inhibitor of a (H^+/K^+) ATPase and a herpetoviridae protease. Nowhere does the cited art, alone or taken together, disclose or suggest a method to treat herpetoviridae infection in a subject by administering a compound that is a dual inhibitor of a (H^+/K^+) ATPase and a herpetoviridae protease.

In light of the foregoing reasons, the Office has failed to establish that claim 1 is *prima facie* obvious in view of EP '217 and Lindberg et al. Moreover, claims 2, 22, 25, 31, 32, and new claim 33, which depend from claim 1, are likewise patent able over these references for the reasons stated with respect to claim 1 and by reason of the additional requirements that they introduce.

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[35]Paper 10 at page 5.

[36]See page 142 of the specification.

[37]See Paper 10 at page 5.

IV. Non-Statutory Double Patenting Rejection

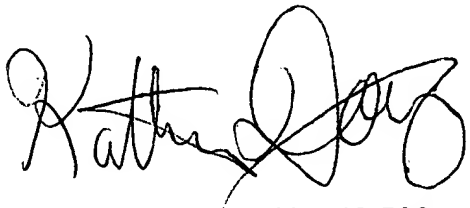
Claims 1,2, 22, 25, and 31-32 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 5,945,425. Applicants have already submitted a terminal disclaimer on December 6, 2002, disclaiming the amount of any patent term on a patent issuing from this application which extends beyond the patent term of U.S. Patent No. 5,945,425. For the Office's convenience, a copy of the terminal disclaimer and certificate under 37 CFR 3.73(b) are enclosed with this response. Applicants, accordingly, respectfully request reconsideration and withdrawal of the non-statutory double patenting rejection.

V. Conclusion

In light of the foregoing, Applicants request entry of the claim amendments, withdrawal of the claim rejections, and solicit an allowance of the claims. The Examiner is invited to contact the undersigned attorney should any issues remain unresolved.

The Commissioner is hereby authorized to charge any underpayment and credit any overpayment of government fees to Deposit Account No. 19-1345.

Respectfully submitted,



Kathryn J. Doty, Reg. No. 40,593
SENNIGER, POWERS, LEAVITT & ROEDEL
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
(314) 231-5400

Express Mail Label No. EV 324378991 US
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